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UTILITY PATENT APPLICATION TRANSMITTAL
(Small Entity)

(Only for new nonprovisional applications under 37 CFR 1.53(b))

Docket No.
1910/174
Total Pages in this Submission
17

TO THE ASSISTANT COMMISSIONER FOR PATENTS
Box Patent Application
Washington, D.C. 20231

Transmitted herewith for filing under 35 U.S.C. 111(a) and 37 C.F.R. 1.53(b) is a new utility patent application for an invention entitled:

IMPROVED PROTEINACEOUS ANIMAL CHEW WITH DENTALLY THERAPEUTIC CATION

and invented by:

R. Eric Montgomery

If a CONTINUATION APPLICATION, *check appropriate box and supply the requisite information:*

☒ **Continuation** ☐ **Divisional** ☐ **Continuation-in-part (CIP)** of prior application No.: 08/689,475

Which is a:

☐ **Continuation** ☐ **Divisional** ☐ **Continuation-in-part (CIP)** of prior application No.: _____

Which is a:

☐ **Continuation** ☐ **Divisional** ☐ **Continuation-in-part (CIP)** of prior application No.: _____

Enclosed are:

Application Elements

1. ☒ Filing fee as calculated and transmitted as described below
2. ☒ Specification having 9 pages and including the following:
   - a. ☒ Descriptive Title of the Invention
   - b. ☒ Cross References to Related Applications *(if applicable)*
   - c. ☐ Statement Regarding Federally-sponsored Research/Development *(if applicable)*
   - d. ☐ Reference to Microfiche Appendix *(if applicable)*
   - e. ☒ Background of the Invention
   - f. ☒ Brief Summary of the Invention
   - g. ☒ Brief Description of the Drawings *(if drawings filed)*
   - h. ☒ Detailed Description
   - i. ☒ Claim(s) as Classified Below
   - j. ☒ Abstract of the Disclosure

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Application Elements (Continued)

3. ☐ Drawing(s) *(when necessary as prescribed by 35 USC 113)*
   a. ☐ Formal b. ☐ Informal Number of Sheets _____

4. ☒ Oath or Declaration
   a. ☐ Newly executed *(original or copy)* ☒ Unexecuted
   b. ☐ Copy from a prior application (37 CFR 1.63(d)) *(for continuation/divisional application only)*
   c. ☒ With Power of Attorney ☐ Without Power of Attorney
   d. ☐ *DELETION OF INVENTOR(S)*
   Signed statement attached deleting inventor(s) named in the prior application, see 37 C.F.R. 1.63(d)(2) and 1.33(b).

5. ☐ Incorporation By Reference *(usable if Box 4b is checked)*
The entire disclosure of the prior application, from which a copy of the oath or declaration is supplied under Box 4b, is considered as being part of the disclosure of the accompanying application and is hereby incorporated by reference therein.

6. ☐ Computer Program in Microfiche

7. ☐ Genetic Sequence Submission *(if applicable, all must be included)*
   a. ☐ Paper Copy
   b. ☐ Computer Readable Copy
   c. ☐ Statement Verifying Identical Paper and Computer Readable Copy

Accompanying Application Parts

8. ☐ Assignment Papers *(cover sheet & documents)*

9. ☐ 37 CFR 3.73(b) Statement *(when there is an assignee)*

10. ☐ English Translation Document *(if applicable)*

11. ☐ Information Disclosure Statement/PTO-1449 ☐ Copies of IDS Citations

12. ☐ Preliminary Amendment

13. ☒ Acknowledgment postcard

14. ☒ Certificate of Mailing
   ☐ First Class ☐ Express Mail *(Specify Label No.):* EL361717708US

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Accompanying Application Parts (Continued)

15. ☐ Certified Copy of Priority Document(s) *(if foreign priority is claimed)*

16. ☒ Small Entity Statement(s) - Specify Number of Statements Submitted: 1 (copy from parent appln)

17. ☐ Additional Enclosures *(please identify below):*

Fee Calculation and Transmittal

CLAIMS AS FILED

For	#Filed	#Allowed	#Extra		Rate	Fee
Total Claims	13	- 20 =	0	x	$18.00	$0.00
Indep. Claims	2	- 3 =	0	x	$78.00	$0.00
Multiple Dependent Claims (check if applicable) ☐						$0.00
					BASIC FEE	$380.00
OTHER FEE *(specify purpose)* _____						
					TOTAL FILING FEE	$380.00

☒ A check in the amount of $380.00 to cover the filing fee is enclosed.

☐ The Commissioner is hereby authorized to charge and credit Deposit Account No. 19-4972 as described below. A duplicate copy of this sheet is enclosed.

- ☐ Charge the amount of as filing fee.
- ☒ Credit any overpayment.
- ☒ Charge any additional filing fees required under 37 C.F.R. 1.16 and 1.17.
- ☐ Charge the issue fee set in 37 C.F.R. 1.18 at the mailing of the Notice of Allowance, pursuant to 37 C.F.R. 1.311(b).

Dated: September 16, 1999

Herbert A. Newborn
Signature

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Atty Dkt: 1910/109

VERIFIED STATEMENT CLAIMING SMALL ENTITY STATUS - INDEPENDENT INVENTOR

Applicant(s): R. Eric Montgomery

Serial No: Not Assigned

Date Filed: Herewith

For: IMPROVED ANIMAL CHEW WITH DENTALLY THERAPEUTIC AGENT

As a below-named inventor, I hereby declare that I qualify as an independent inventor as defined in 37 CFR 1.9(c), for purposes of paying reduced fees under Section 41(a) and (b) of Title 35, United States Code with regard to the above invention.

I have not assigned, granted, conveyed, or licensed, and am under no obligation under contract or law to assign, grant, convey, or license, any rights in the invention to any person who could not be classified as an independent inventor under 37 CFR 1.9(c) if that person had made the invention, or to any concern which would not qualify as a small business concern under 37 CFR 1.9(d) or a nonprofit organization under 37 CFR 1.9(e).

Each person, concern, or organization to which I have assigned, granted, conveyed, or licensed or am under an obligation under contract or law to assign, grant, convey, or license any rights in the invention is listed below:

_____

(individual, small business concern, nonprofit organization)

I acknowledge the duty to file, in this application, notification of any change in status resulting in loss of entitlement to small entity status prior to paying, or at the time of paying, the earliest of the issue fee or any maintenance fee due after the date on which status as a small business entity is no longer appropriate.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the

application, any patent issuing thereon, or any patent to which this verified statement is directed.

Inventor: R. Eric Montgomery

Signature: R. E. Montgomery

Date: 8-11-95

[jr22:1910109.ind]

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICATION FOR UNITED STATES PATENT

for

IMPROVED PROTEINACEOUS ANIMAL CHEW WITH DENTALLY THERAPEUTIC CATION

Inventor: **R. Eric Montgomery**
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Attorney Docket: 1910/174

IMPROVED PROTEINACEOUS ANIMAL CHEW WITH DENTALLY THERAPEUTIC CATION

Related U.S. Application(s)

This application is a continuation of U.S. application Serial No. 08/689,475, filed August 15, 1996 that claims priority from U.S. provisional application Serial No. 60/002,345, filed August 15, 1995. Both of these related applications are hereby incorporated herein by reference.

Technical Field

The invention is directed to methods and compositions for delivery of therapeutic agents to an animal by oral administration.

Background art

It is known that the dental health of dogs or other domestic animals is often deficient owing to the impossibility of achieving an effective brushing of their teeth with suitable dental products in a way comparable to that in humans.

A number of therapeutic proteinaceous animal chews have been described in the prior art to address this problem. The therapeutic effect from these prior art compositions or devices comes primarily from the physical act of chewing an object to provide an abrasive effect on the teeth prior to swallowing the compositions. The act of regularly chewing an object (such as rawhide) sufficiently rigid to allow for an oral residence time of greater than thirty seconds or so has been shown to result in reduced tartar accumulation compared to a quickly consumable object, such as a biscuit (Lags, et al J. Am. Veterinary Medical Ass, 197, pp 213-219 (1990)).

Simone et al. US patent No 5,296,209, reported on an attempt to clean an animal's teeth through providing a foodstuff with a texture that allows for the animals tooth, during the act of chewing, to penetrate relatively deep into the food particle before it breaks apart into smaller particles. By doing so, the tooth surface is mechanically abraded by the food particle for a longer period of time than would be possible with a hard, readily breakable food particle. The disadvantage to this approach to companion animal dental hygiene is that only physical accumulation such as tartar, and perhaps some plaque structure, are removed. There is little offered in the way of a truly therapeutic or preventative effect.

These animal chews may in certain instances contain therapeutic compositions in addition to the chew itself. Compositions that have been incorporated into the animal chew may be identified as belonging to one of two categories. The first category is that of enzymatic compositions exemplified by Montgomery US patent 5,310,541. Enzymatic compositions have been found to have limited antimicrobial effect. The second category is that of non-enzymatic compositions associated with the animal chews.

For example, Stacey , US Patent No 5,296,217, described the use of a hexametaphosphate salt added to a consumable animal treat or foodstuff in order to prevent tartar accumulation in domestic animals. Not only is the residence time of the salt too short to have a significant therapeutic effect in the oral cavity of the animal, but furthermore, the hexametaphosphate is not antimicrobial. In Spanier et al., US patent Nos 5, 114,704 and 5,011,679, a rawhide carrier coated with an inorganic pyrophosphate compound was described for purposes of preventing tartar accumulation in dogs. Pyrophosphate is a calcium chelator that limits the accumulation of tartar and reduces the tartar build-up that has occurred. However, this composition lacks antimicrobial properties.

There are a number of cationic antimicrobial agents that have been utilized in

toothpastes for human dental care. These agents strongly associate with protein and are not readily released from proteinaceous substrates.

There is an unmet need for an animal chew that has effective antimicrobial properties in the oral cavity of an animal.

Summary of the Invention

The invention satisfies the above need. A novel animal oral care composition is provided that includes a carrier having a negatively-charged surface and an effective dose of a therapeutic composition for achieving antimicrobial activity in the oral cavity of the animal, wherein the therapeutic composition contains at least a cationic antimicrobial substance and is in a saliva soluble form positioned close to or at the surface of the proteinaceous carrier. A method is further provided for providing dental health in an animal, including obtaining an animal oral care composition as described above and administering the composition to the animal in a form that will be voluntarily chewed by the animal.

Detailed Description

The invention provides a composition and method directed to the dental health and well-being of animals and includes the following features. Firstly, the composition is safe for consumption, much as a foodstuff or animal feed would be; secondly, human intervention is not required in the companion animal oral care process; thirdly, in order to satisfy the self-administration rule, the composition in association with a carrier, is sufficiently palatable for the animal to maintain its interest in consuming the material; fourthly, the residence time of the composition and the carrier is sufficient to permit the desired therapeutic effect; and fifthly the therapeutic substance is readily released into saliva upon being chewed.

The present invention has accomplished all these criteria in a novel formulation. According to the invention, a carrier is utilized that has a negative surface charge. The carrier may be formed from natural or synthetic substances, and further may be inherently negatively charged, or may be coated by a reagent that imparts the negative charge to the surface of the carrier. The carrier should persist in the oral cavity of the animal for a minimum residence time of at least 1 minute. Furthermore, the carrier itself should be palatable for the animal such that the interest of the animal in the carrier is maintained.

The carrier provides a means for introducing the therapeutic agent into the oral cavity. The therapeutic substance is located on or near the surface of the chewable object in order for intimate contact between the moisture of saliva and the therapeutic substance to occur almost immediately upon the start of the chewing cycle so as to minimize the possibility that the therapeutic substance will be consumed with the chew, rather than being released in to the oral cavity.

An embodiment of the invention describes a formulation that utilizes a proteinaceous animal chew such as rawhide, and a dentally therapeutic cation, (in this example, chlorhexidine) that is maintained on the surface of the chew on the basis of charge attraction. The cationic antimicrobials become strongly bound to negatively-charged surfaces containing negatively charged moieties such as carboxylic, phosphate and sulfate moieties by forming salt bridges. Cationic antimicrobials that are released from the carrier in the presence of saliva are observed to have a long duration of action, due to their retention and adherence to the negatively-charged surface in the oral cavity, e.g., enamel hydroxyapatite, acquired pellicle protein, and the oral mucosa.

In a preferred embodiment, the cation is rapidly solubilized in the saliva of the oral cavity when the cation is combined with or deposited on the chew in the presence of an alkali metal salt such as sodium gluconate. It has unexpectedly been

found that the presence of the alkali metal salt effectively prevents the cationic compound from precipitating or otherwise adhering to the proteinaceous carrier, thus rendering it readily soluble in saliva during the chewing cycle. The invention is not limited to a solubilization process that utilizes an alkali metal salt. Alternative secondary agents are contemplated that provide a means to readily release cations into saliva. Thus, the therapeutic cation is released into the salivary solution during the chewing cycle, rather than carried into the intestinal tract as a result of being bound irreversibly to the carrier.

Cationic antimicrobials contemplated to have utility in the invention include chlorhexidine diacetate, chlorhexidine digluconate, cetylpyridinium chloride, domiphen bromide, benzalkonium chloride, benzethonium chloride, and alexidene.

Alkali metal salts having utility in the invention include sodium and potassium salts of hydrochloric acid, hydrobromic acid, gluconic acid, and acetic acid.

Auxiliary ingredients such as flavorants and film-forming agents may be included in the compositions to provide a specific palatability or coating effect respectively. In particular, film formers such as hydroxypropylcellulose, carrageenan and polyvinylpyrrolidone may provide for a more uniform coating of the carrier surface with the inventive compositions. The auxiliary ingredients are not essential for the practice of the invention.

An example of the inventive composition is prepared as follows:

EXAMPLES

EXAMPLE 1 : Preparation of a rawhide chew having antimicrobial activity.

5 lbs of dried rectangular rawhide chews were basted with the following solution using a spray bottle:

Chlorhexidine digluconate	24 grams
sodium gluconate	24 grams
deionized water	952 grams

The chews were coated at a rate of approximately 114 grams of basting solution per 5 lbs of rawhide. The resulting wet basted chews were dried at 40°C for 24 hours and subsequently placed in airtight bags.

EXAMPLE 2: Assay demonstrating rapid solubilization of the therapeutic composition.

Rawhide chews (10 grams cut into squares of approximately 1/4" on each side) containing the therapeutic composition (e.g., chlorhexidine) were placed in distilled water (20 mls) shaken for 60 seconds, and the resulting filtrate assayed for the presence of chlorhexidine in solution by infrared spectroscopy. Over 80% (0.486 mg/ml) of the theoretical soluble chlorhexidine (0.6mg/ml) was found in solution. A rawhide chew basted with a solution containing chlorhexidine digluconate but without sodium gluconate showed a soluble chlorhexidine level of only 0.03mg/ml.

EXAMPLE 3: Use of different carriers for delivery of a therapeutic agent

Using the assay in Example 2, the therapeutic composition is shown to be effective when administered with a proteinaceous carrier such as a rawhide chew or a food stuff, and furthermore the food stuff may be composed either wholly or partly of protein.

I claim:

1. An animal oral care composition comprising:

(a) a carrier having a negatively charged surface obtaining an animal oral care composition andadministering the composition to the animal in a form that will be voluntarily chewed by the animal; and

(b) an effective dose of a therapeutic composition for achieving activity in the oral cavity of the animal, wherein the therapeutic composition contains at least a cationic antimicrobial substance and is in a saliva soluble form positioned close to or at the surface of the carrier.

2. A composition according to claim 1, wherein the therapeutic composition contains a counterion in addition to the cationic antimicrobial substance.

3. A composition according to claim 2, wherein the counterion is selected from the group consisting of sodium and potassium salts of hydrochloric acid, hydrobromic acid, gluconic acid, and acetic acid.

4. A composition according to claim 1, wherein the cationic antimicrobial agent is selected from the group consisting of chlorhexidine diacetate, chlorhexidine digluconate, cetylpyridinium chloride, domiphen bromide, benzalkonium chloride, benzethonium chloride, and alexidene.

5. A composition accoridng to claim 2, wherein the cationic microbial substance is chlorhexidine and the counterion is sodium gluconate.

6. A composition according to claim 1, wherein the carrier is a proteinaceous carrier.

7. A composition according to claim 6, wherein the proteinaceous carrier is a rawhide chew.

8. A method for providing dental health in an animal comprising:

(a) obtaining an animal oral care composition; and

(b) administering the composition to the animal in a form that will be voluntarily chewed by the animal.

9. A method according to claim 8, wherein the therapeutic composition contains a counterion in addition to the cationic antimicrobial substance.

10. A method according to claim 9, wherein the counterion is selected from the group consisting of sodium and potassium salts of hydrochloric acid, hydrobromic acid, gluconic acid, and acetic acid.

11. A method according to claim 8, wherein the cationic antimicrobial agent is selected from the group consisting of chlorhexidine diacetate, chlorhexidine digluconate, cetylpyridinium chloride, domiphen bromide, benzalkonium chloride, benzethonium chloride, and alexidene.

12. A method according to claim 11, wherein the cationic microbial substance is chlorhexidine and the counterion is sodium gluconate.

13. A method according to claim 8, wherein the proteinaceous carrier is a rawhide chew.

Abstract

This invention relates to chewable objects for animals which contain, as a dentally therapeutic ingredient, one or more cationic substances. The inventive therapeutic animal chews are of sufficient durability to allow for a chewing cycle long enough for the release of the aforementioned cationic substances into saliva. Furthermore, the inventive animal chews may contain an effective amount of a counter-ionic compound, such as an alkali metal salt, to allow for rapid solubilization of said cationic antimicrobial substance into the saliva of an animal chewing thereupon, especially when delivered or carried on a carrier having a negatively charged surface.

97591

Docket No.
1910/174

Declaration and Power of Attorney For Patent Application

English Language Declaration

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name,

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled

IMPROVED PROTEINACEOUS ANIMAL CHEW WITH DENTALLY THERAPEUTIC CATION

the specification of which

(check one)

☒ is attached hereto.

☐ was filed on _____ as United States Application No. or PCT International Application Number _____

and was amended on _____

(if applicable)

I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose to the United States Patent and Trademark Office all information known to me to be material to patentability as defined in Title 37, Code of Federal Regulations, Section 1.56.

I hereby claim foreign priority benefits under Title 35, United States Code, Section 119(a)-(d) or Section 365(b) of any foreign application(s) for patent or inventor's certificate, or Section 365(a) of any PCT International application which designated at least one country other than the United States, listed below and have also identified below, by checking the box, any foreign application for patent or inventor's certificate or PCT International application having a filing date before that of the application on which priority is claimed.

Prior Foreign Application(s)			Priority Not Claimed
_____ (Number)	_____ (Country)	_____ (Day/Month/Year Filed)	☐
_____ (Number)	_____ (Country)	_____ (Day/Month/Year Filed)	☐
_____ (Number)	_____ (Country)	_____ (Day/Month/Year Filed)	☐

I hereby claim the benefit under 35 U.S.C. Section 119(e) of any United States provisional application(s) listed below:

60/002,345	August 15, 1995
(Application Serial No.)	(Filing Date)
(Application Serial No.)	(Filing Date)
(Application Serial No.)	(Filing Date)

I hereby claim the benefit under 35 U. S. C. Section 120 of any United States application(s), or Section 365(c) of any PCT International application designating the United States, listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States or PCT International application in the manner provided by the first paragraph of 35 U.S.C. Section 112, I acknowledge the duty to disclose to the United States Patent and Trademark Office all information known to me to be material to patentability as defined in Title 37, C. F. R., Section 1.56 which became available between the filing date of the prior application and the national or PCT International filing date of this application:

08/689,475	August 15, 1996	Allowed
(Application Serial No.)	(Filing Date)	(Status) (patented, pending, abandoned)
(Application Serial No.)	(Filing Date)	(Status) (patented, pending, abandoned)
(Application Serial No.)	(Filing Date)	(Status) (patented, pending, abandoned)

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

POWER OF ATTORNEY: As a named inventor, I hereby appoint the following attorney(s) and/or agent(s) to prosecute this application and transact all business in the Patent and Trademark Office connected therewith. *(list name and registration number)*

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Second inventor's signature Date
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